Attachment 2: Literature Review

Author	Journal or Book	Year	Type of Study	Outcomes Studied	Patient	Results	HCFA Comments
Al-Assi MT, Miki K, Walsh J, Graham DP, Asaka M, Graham DY	*American Journal of Gastroenterology*	1999	Diagnostic trial	Prospective evaluation of several biochemical markers, including serum IgG antibodies (but not HpSA) as markers for post-therapeutic	Not applicable to clinical utility of current request.	Not applicable to clinical utility of current request.	Reported negative results on the effectiveness of H. pylori serum antibody testing does not directly contribute to the evaluation of the clinical utility of HpSA: It merely highlights the weaknesses of another, yet somewhat comparable, approach to evaluating post-therapeutic eradication.
Blaser M	*Journal of Infectious Diseases*	1999	Review article	Not applicable to clinical utility of current request.	Not applicable to clinical utility of current request.	Not applicable to clinical utility of current request.	Discussion on the "ecology" of H. pylori within the gastrointestinal tract, and potential effects of eradication upon this microbial balance.
Bravo L, Realpe J, Campo C, Mera R, Correa P	*American Journal of Gastroenterology*	1999	Diagnostic trial	Prospective study on role of acid suppression and bismuth on performance of urea breath test (UBT) vs. HpSA.	60 patients with previous diagnoses of atrophic gastritis and H. pylori infection who were participating in an ongoing study of gastric pre-malignant lesions.	1. Ranitidine: UBT nor HpSA affected. 2. Lansoprazole: UBT showing 30-40% false-negatives (FN), with HpSA 15-25% FN. 3. Bismuth: UBT 45-55% FN, with HpSA 10-15% FN.	Data suggests that HpSA may confer somewhat of a diagnostic advantage over UBT with respect to assaying patients on selected medications, but the Discussion section also noted that "in both tests, the effects of lansoprazole and bismuth are nullified 2 wk after removal of the medication."

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Centers for Disease Control and Prevention	*Fact Sheet for Physicians*	1997	Physician Fact Sheet	Not applicable to clinical utility of current request	Not applicable to clinical utility of current request	Not applicable to clinical utility of current request	Useful pointers for practicing physicians including indications: 1. Signs and symptoms consistent with active gastric or duodenal ulcers 2. Following resection of early gastric cancer 3. For low-grade gastric MALT lymphoma
Cutler A, Havstad S, Ma CK, Blaser MJ, Perez-Perez G, Schubert T	*Gastroenterology*	1995	Diagnostic trial	Comparative performance of multiple laboratory markers (not including HpSA) for primary diagnosis.	Not applicable to clinical utility of current request.	Not applicable to clinical utility of current request.	Only of background relevance for this formal request.
Cutler A, Prasad V	*American Journal of Gastroenterology*	1996	Diagnostic trial	Assessment of serum serology (not including HpSA) in evaluation of H. pylori	Not applicable to clinical utility of current request.	Not applicable to clinical utility of current request.	Not directly pertinent to current coverage request, although article does provide evidence on the inability for qualitative serum serology to be an effective serial marker for assessing successful eradication.
Eslick G, Lim L, Byles J, Xia H, Talley N	*American Journal of Gastroenterology*	1999	Meta-analysis	Pooling published data on the epidemiological association of H. pylori with gastric CA.	Not applicable to clinical utility of current request.	Not applicable to clinical utility of current request.	Pooled data 2-fold risk of developing H. pylori infection in developing gastric cancer is background information only with respect to current coverage request.

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Feldman M, Cryer B, Lee E, Peterson W	*Journal of American Medical Association*	1998	Diagnostic trial	Role of serum serologic testing to confirm cure of H. pylori infection following antimicrobial therapy.	23 otherwise healthy men and women (mean age 49) with active H. pylori infection documented by gastric biopsy and positive serology.	At 18 months following therapy, sensitivity of seroconversion in detecting cure (that is, positive to negative result) = 60% and specificity = 100%, using histologic gold standard.	Demonstrates inability of serum serology to serve as a definitive diagnostic marker for successful
Fennerty MB	*Laboratory Medicine*	1998	Review article	Reviews multiple diagnostic tests for H. pylori, not including HpSA.	Not applicable to clinical utility of current request.	Not applicable to clinical utility of current request.	Only of background relevance for this formal request.
Fraser A, Ali MR, McCullough S, Yeates N, Haystead A	*New Zealand Medical Journal*	1996	Diagnostic trial	Prospective study using interview data from patients (e.g., symptoms, use of non-steroidal anti-inflammatory drugs) in which clinical diagnosis was matched against endoscopic diagnosis and H. pylori status (using serum serology with urea breath test and histologic CLO test for confirmation).	436 consecutive patients presenting for upper endoscopy.	Table 1 summarizes cross-tabulation of endoscopic diagnosis with H. pylori status. Flowchart in Fig. 4 suggests role of H. pylori testing in the follow-up endoscopic evaluation of the patient with dyspepsia: This diagram illustrates relationship of serum serology with endoscopic diagnoses for the 351 patients who presented with either reflux or dyspepsia.	Although HpSA is not included in this study, it still presents useful information on the clinical utility of H. pylori testing.

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Makristathis A, Pasching E, Schütze K, Wimmer M, Rotter M, Hirschl A	*Journal of Clinical Microbiology*	1998	Diagnostic trial	Comparative performance of HpSA against polymerase chain reaction (PCR) assay.	63 H. pylori-infected adults with duodenal ulcers and 37 non-infected persons, who were chosen to approximate 63% expected prevalence of H. pylori experienced by the study's medical center. 55/63 patients evaluated for follow-up eradication control 35 days after the start of treatment.	Refer to Table 1 for complete 2x2 data: 1. For primary diagnosis, HpSA: SENS=88.9%, SPEC=94.6% PCR: SENS=93.7%, SPEC=100% 2. For eradication evaluation, HpSA: SENS=85.7%, SPEC=68.3% PCR: SENS=92.9%, SPEC=48.8%	Illustrates comparable performance data of HpSA compared against another emerging diagnostic test (PCR serving as a representative molecular-based diagnostic test). Please note, however, that there is a study design concern with respect to the formulation of a working confirmatory gold standard since two different assay systems are used to prove positive and negative H. pylori status, respectively (that is, positive status proven by histology and culture, whereas negative status was proven by urea breath test and serology).

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Mégraud F	*Gastroenterology*	1997	Review article	Comparative performance of multiple laboratory markers for both primary diagnosis and evaluation of eradication.	Not applicable to clinical utility of current request.	Not applicable to clinical utility of current request.	Although there is not discussion of HpSA, Fig. 1 illustrates a possible protocol for laboratory + follow-up endoscopic evaluation. Article also raises issue of emerging markers such as salivary IgG and the CagA protein, the latter of which may serve as a potential genotypic predictor of more severe disease. Finally, a follow-up Commentary by Peter Malfertheiner the same December 1997 Gastroenterology Supplement (S118-S-119) highlights that although the precise clinical indications for choosing to diagnose H. pylori have not achieved broad consensus, "treatment is still not in the state of broad preventive use and therefore testing should not be propagated in asymptomatic individuals without particular anamnestic or other risk conditions."

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National Institute of Diabetes and Digestive and Kidney Diseases	*http://www.niddk.nih.gov/StomachUlcers/Ulcers.html*	1996	Review Article	Not applicable to clinical utility of current request.	Not applicable to clinical utility of current request.	Not applicable to clinical utility of current request.	General background only on pathophysiology of H. pylori, without direct benefit to assessing HpSA
National Institutes of Health	*NIH Consensus Statement*	1994	Review article	Not applicable to clinical utility of current request.	Not applicable to clinical utility of current request.	Not applicable to clinical utility of current request.	General background only on pathophysiology of H. pylori, without direct benefit to assessing HpSA
Rollán A, Giancaspero R, Arrese M, Figueroa C, Vollrath V, Schultz M, et al	*American Journal of Gastroenterology*	1997	Diagnostic trial	Assessment of seven diagnostic markers (not including HpSA) in evaluation of H. pylori eradication.	Not applicable to clinical utility of current request.	Not applicable to clinical utility of current request.	Not directly pertinent to current coverage request, although article does provide evidence on the ability of urea breath test to be an effective marker for assessing successful eradication.
Soll A	*Journal of American Medical Association*	1996	Review article	Formulation of practice guidelines from Practice Parameters Committee of the American College of Gastroenterology.	Not applicable to clinical utility of current request.	Not applicable to clinical utility of current request.	Although non-contributory with respect to HpSA, these guidelines suggest options for H. pylori diagnosis in dyspeptic patients.
Sternberg A, Coscas D, Wagner Y, Auslander L, Kaufshtein M, Fireman Z	*Israeli Journal of Medical Science*	1997	Diagnostic trial	Prospective comparison of culture, histology and serology (serum only, not including HpSA).	Not applicable to clinical utility of current request.	Not applicable to clinical utility of current request.	Only of background relevance for this formal request.

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Thijs JC, Zwet AA van, Thijs WJ, Oey HB, Karrenbeld A, Stellaard F, et al	*American Journal of Gastroenterology*	1996	Diagnostic trial	Prospective comparison of six diagnostic tests, not including HpSA.	Not applicable to clinical utility of current request.	Not applicable to clinical utility of current request.	Only of background relevance for this formal request.
Trevisani L, Sartori S, Galvani F, Rossi MR, Ruina M, Chiamenti C, et al	*American Journal of Gastroenterology*	1999	Diagnostic trial	Performance of HpSA for primary diagnosis and evaluating post-treatment	270 patients (155 males, 115 females with mean age 56) referred for esophagogastroduodenoscopy (EGDS): Group A (n=154) - Upper GI symptoms without prior H. pylori diagnosis and treatment Group B (n=116) - Undergoing EGDS two months following eradication therapy	Refer to Table 1: 1. For primary diagnosis (Group A): SENS=94% (87-98) SPEC=90% (80-96) 2. For eradication evaluation Group B): SENS=93% (81-99) SPEC=82% (71-90) NOTE: 12/13 patients with false-positive HpSA results agreed to undergo repeat urea breath tests (UBT) and HpSA 2-6 months after first evaluation: 11/12 cases UBT negative, with 8/11 HpSA remaining positive and 3/11 reverting to negative.	1. Gold standard = Histology + Rapid Urease Test, with both tests needing to be positive or both tests needing to be negative. 2. Based upon the presence of considerable false-positive results in Group B, the authors concluded that HpSA "appears less suitable to evaluate the outcome of the eradicating treatment."

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Vaira D, Malfertheiner P, Megraud F, Axon A, Deltenre M, Hirschl A, et al	*Lancet*	1999	Diagnostic trial	Prospective evaluation of stool specimens using HpSA vs. carbon-13-urea breath test (UBT).	501 patients (276 men, 225 women with mean age 52) from eleven European medical centers, who would be undergoing gastroscopy, with 107 patients available for post-treatment evaluation.	1. For primary diagnosis, HpSA: SENS=94.1% (90.6-96.6); SPEC=91.8% (87.3-95.1) UBT: SENS=95.3% (92.2-97.5); SPEC=97.7% (94.8-99.3) 2. For eradication evaluation, HpSA: SENS=90.0% (68.3-98.8); SPEC=95.3% (88.5-98.7) UBT: SENS=90.0% (68.3-98.8); SPEC=98.9% (93.8-100.0)	1. Please note comparable performance of both UBT and HpSA, although this study did not pertain to clinical utility of such testing. 2. Gold standard used EITHER histology + urease results OR culture only.
Wilcox MH, Dent THS, Hunter JO, Gray JJ, Brown DFJ, Wight DGD, et al	*Journal of Clinical Pathology*	1996	Diagnostic trial	Prospective comparison of eight serum serology kits (not including HpSA).	Not applicable to clinical utility of current request.	Not applicable to clinical utility of current request.	Only of background relevance for this formal request.